

Application No. 10/089,742
Applicant(s): Brosens, Jan
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IN THE CLAIMS

Please cancel claims 1-17 without prejudice and add the following new claims ^{24 46}18-40 as follows:

²⁴
~~18~~. A genetic construct which comprises a nucleotide sequence of interest (NOI) and splice-functional element(s) selected and arranged such that the first open reading frame (ORF) available for translation in a target cell population is for the NOI while in non-target cells the NOI ORF is absent or is not the primary ORF.

²⁵
~~19~~. A construct as claimed in claim 18 wherein the protein expression product of the NOI is generated by a *cis*-splicing mechanism.

²⁶
~~20~~. A construct as claimed in claim 18 wherein the NOI is a therapeutic gene.

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~~21~~. A construct as claimed in claim 20 wherein the NOI encodes a cytotoxic agent.

²⁸
~~22~~. A construct as claimed in claim 18 wherein the target cell population is a malignant cell population.

²⁹
~~23~~. A construct as claimed in claim 18 wherein the NOI is not expressed as a fusion product with one or more exons or partial exons from within the splice-functional elements.

³⁰
~~24~~. A construct as claimed in claim 18 wherein said splice-functional elements include the B-tropomyosin exon 5 splice donor and/or the B-tropomyosin exon 7 splice acceptor.

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³¹
~~25~~. A construct as claimed in claim 18 wherein said splice-functional elements include human FGFR α -exon.

³²
~~26~~. A construct as claimed in claim 25 wherein the target cell population comprises glioblastoma related/ derived cells.

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~~27~~. A construct as claimed in claim 18 wherein the splice-functional elements include the mitochondrial ATP synthase γ subunit.

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~~28~~. A construct as claimed in claim 18 wherein the splice-functional elements include regions from within the human non-muscle myosin heavy chain B.

³⁵
~~29~~. An mRNA molecule derived from a genetic construct as defined in claim 18.

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~~30~~. A protein molecule obtained by expression of a genetic construct as defined in claim 18.

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~~31~~. A vector incorporating a genetic construct as claimed in claim 18.

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~~32~~. A cell comprising a construct, nucleic acid or protein molecule or vector as claimed in claim 18.

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~~33~~. A construct or vector as claimed in claim 18 for use in therapy.

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~~34~~. Use of a construct or vector as claimed in claim 18 in the manufacture of a medicament whose physiological effect is restricted to a target cell population and which treats a disease characterised in that it is responsive to expression of an exogenously administered gene.

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41
35. A pharmaceutical formulation comprising a construct or vector as claimed in claim 18 in admixture with a physiologically acceptable diluent or carrier.

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36. A method of selectively expressing a nucleotide sequence of interest (NOI) in a target cell population which comprises introducing into said cell population an alternatively spliced molecule which incorporate said
NOI.

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37. A method as claimed in claim 36 wherein said alternatively spliced molecule is also introduced into cells not within the target cell-population.

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38. A method as claimed in claim 36 wherein splice-functional elements within the alternatively spliced molecule direct target and non-target cells to generate, though *cis*-splicing, different mature mRNA molecules.

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39. A method as claimed in claim 36 wherein the NOI expression product is not fused with any exons or partial exons from within the splice-functional elements.

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40. The use of splice-functional elements to restrict translation or expression of a nucleotide sequence of interest to specific cell types and/or environments.